



Beliefs Around Hypoglycemia and Their Impacts on Hypoglycemia Outcomes in Individuals with Type 1 Diabetes and High Risks for Hypoglycemia Despite Using Advanced Diabetes Technologies

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OBJECTIVE

This study aimed to 1) identify the frequency of severe and level 2 hypoglycemia presenting in individuals with type 1 diabetes using continuous glucose monitoring systems (CGMs), including those with concomitant closed-loop insulin pumps, in a clinical practice setting and 2) evaluate the impact of beliefs around hypoglycemia in the development of severe and level 2 hypoglycemia in this population.

RESEARCH DESIGN AND METHODS

A cross-sectional survey study in adults with type 1 diabetes using CGMs >6 months was conducted at a large tertiary academic center. Participant demographics, 6-month severe hypoglycemia history, hypoglycemia beliefs (with the Attitude to Awareness of Hypoglycemia questionnaire), and 4-week CGM glucose data were collected. Statistical analysis was performed to assess the presentation of severe and level 2 hypoglycemia and identify associated risk factors.

RESULTS

A total of 289 participants were recruited (including 257 participants with CGM data within the last 3 months). Of these, 25.6% experienced at least one severe hypoglycemic episode in the last 6 months, and 13.6% presented with ≥1% of time in level 2 hypoglycemia on CGMs. Reporting beliefs about prioritizing hyperglycemia avoidance was associated with severe hypoglycemia development ($P < 0.001$), while having beliefs of minimal concerns for hypoglycemia was associated with spending ≥1% of time in level 2 hypoglycemia ($P = 0.038$).

CONCLUSIONS

Despite the use of advanced diabetes technologies, severe and level 2 hypoglycemia continues to occur in individuals with type 1 diabetes and high hypoglycemia risks. Human factors, including beliefs around hypoglycemia, may continue to impact the effectiveness of glucose self-management.

Individuals living with type 1 diabetes need to face and manage the acute and potentially lethal threat of hypoglycemia on a daily basis (1). People with type 1

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diabetes lose counterregulatory mechanisms, including a physiologic decrease in insulin level and glucagon secretion (2). Furthermore, those who have experienced antecedent hypoglycemic episodes could have diminished or complete loss of hypoglycemic symptoms (a condition termed impaired awareness of hypoglycemia [IAH]) and attenuated adrenal responses to hypoglycemia (2). When losing all these hypoglycemia counterregulatory mechanisms, these individuals are exposed to a >25-fold increased risk for developing dangerous hypoglycemia (2).

More recent evidence have also revealed that behavioral counterregulatory mechanisms associated with cognitive and environmental determinants of hypoglycemia self-management play key roles in the recovery from hypoglycemia in individuals with type 1 diabetes (3–5). Specifically, beliefs around hypoglycemia in individuals with type 1 diabetes and IAH were determined (3) and subsequently used to develop the Attitudes to Awareness of Hypoglycemia (A2A) questionnaire (4). The A2A questionnaire was later validated by the finding that those scoring higher on hypoglycemia-related belief statements had greater risks for developing dangerous hypoglycemia. Additional barriers to hypoglycemia self-management, such as emotional (e.g., self-management burnout, fear of weight gain), action planning (not having rescue treatment on hand/nearby), educational (choosing slow-acting treatment), and social (fear of drawing unwanted attention to oneself) factors have also been identified in individuals with type 1 diabetes (5).

Diabetes technologies have been developed to support diabetes management (6), including continuous glucose monitoring systems (CGMs), which provide real-time glucose information and a customizable glucose alarm system that generates alerts for impending or ongoing hypoglycemia (7). Closed-loop insulin pumps (8), based on glucose information transmitted from CGMs, can automatically decrease or increase basal insulin doses or suspend insulin infusion completely to help achieve goal glucose levels. These insulin pumps also calculate and suggest bolus doses for meals or correcting high glucose levels; pump users can always override the insulin dose if higher or lower doses are determined. These advanced diabetes

technologies have been demonstrated to reduce hypoglycemia (9–11), and CGM use is now considered to be a standard of care for individuals with type 1 diabetes (6).

In 2017, professional diabetes communities published new guidelines on defining hypoglycemia (6,12,13). While hypoglycemia continued to be defined as blood glucose levels <70 mg/dL, blood glucose levels between 54 and 69 mg/dL (3.0–3.8 mmol/L) were redefined as level 1 hypoglycemia. Level 2 hypoglycemia, defined as blood glucose levels <54 mg/dL (<3.0 mmol/L), was deemed particularly important because of its relationship with brain dysfunction, development of IAH and impaired adrenal response to hypoglycemia (2), potentially lethal cardiac arrhythmia (14), and prothrombotic state (15). Severe hypoglycemia (or level 3 hypoglycemia), a clinical event where people develop “altered mental and/or physical status requiring assistance” in hypoglycemia management (12), is associated with increased risks of cardiovascular events and death (16–18). With the growing use of CGMs (19) and emerging outcome data associated with their use, the recommended blood glucose levels for optimal daily diabetes management were further refined in 2019 to target spending $\geq 70\%$ of time between 70 and 180 mg/dL (20) and to spending <4% of time in hypoglycemia and <1% of time in level 2 hypoglycemia (with stricter goals for those with high risks for developing major complications from hypoglycemia) (20). The recommended target hemoglobin A_{1c} (HbA_{1c}) level for individuals with type 1 diabetes is <7% without significant hypoglycemia (21).

With advancements in diabetes technologies, it remains unknown whether human factors continue to affect hypoglycemia development and the achievement of hypoglycemia management goals (22). The current study aimed to address these questions by 1) identifying how severe and level 2 hypoglycemia presents in individuals with type 1 diabetes using CGMs, including those with concomitant closed-loop insulin pumps, in a clinical practice setting and 2) evaluating the impact of beliefs around hypoglycemia in the development of severe and level 2 hypoglycemia in this population.

RESEARCH DESIGN AND METHODS

A cross-sectional survey study was conducted at the University of Michigan from January to April 2021. The study was approved by the University of Michigan Institutional Review Board (HUM00189672). The study involved 1) a self-report survey conducted through REDCap (23), 2) collection of demographic and diabetes-related data through review of electronic medical records (EMRs), and 3) collection of CGM data from EMRs or participants. Survey invitations were sent to 1,024 individuals with a diagnosis of type 1 diabetes and documentation of CGM refills within the last year based upon the University of Michigan EMR. E-mail invitations were sent through the REDCap participant recruitment tool. For people who did not have an e-mail address listed in the EMR or were found to have an invalid e-mail address, telephone calls were generated or physical letters were mailed to recruit participants. Participants were encouraged to complete the survey on the REDCap website. For those who did not have immediate access to the Internet or had difficulty reading the questions, the study team assisted the participants to complete the questionnaire by telephone. The investigators did not intentionally recruit their own patients to avoid selection bias and implied risk of coercion. All participants provided informed consent before participating in study activities.

Study Survey

The survey assessed durations of diabetes and CGM use, insulin pump use and pump features (e.g., insulin auto-suspension feature [“Does your insulin pump automatically stop insulin infusion if your CGM glucose runs low?”] and closed-loop feature [“Does your insulin pump automatically change insulin dose based on high or low glucose levels on CGM?”]), and development of severe hypoglycemia in the last 6 months (“In the past 6 months, how many times have you had severe hypoglycemia [hypoglycemia events where you need someone to help you take treatment to recover from low glucose levels]?”). Hypoglycemia awareness status was assessed through the Gold et al. (24) questionnaire, which asks individuals to report their experience in detecting hypoglycemic events with scores ranging from 1 (always aware) to 7 (never

aware) in a Likert-type scale. A score ≥ 4 indicates IA, a score ≤ 2 indicates normal hypoglycemia awareness, and a score of 3 represents undetermined awareness status. The A2A questionnaire (4) for assessing patient beliefs around hypoglycemia consists of 12 attitudinal statements reflecting three themes: asymptomatic hypoglycemia normalized, hypoglycemia concerns minimized, and hyperglycemia avoidance prioritized. Respondents rate their levels of agreement on a Likert scale ranging from 0 (not at all true) to 3 (very true) to generate a score for each statement. Summary scores for each theme were calculated by adding scores on the attitudinal statements within the themes.

EMR Review and CGM Data Collection

Participants' EMRs were reviewed to collect information on demographics (age, sex, race, ethnicity), CGM type, insulin pump type, and most recent HbA_{1c} level, BMI, and estimated glomerular filtration rate (eGFR). Four-week CGM summary data (25) within 3 months prior to survey completion were collected from EMRs. For those without recent CGM data in the EMR, follow-up e-mails or telephone calls were conducted to collect CGM data directly from the participants. CGM glucose measures (20), including the percentage of time spent with glucose levels >180 and >250 mg/dL and <70 and <54 (50 for Medtronic CGMs) mg/dL and percentage of time in range (glucose levels between 70 and 180 mg/dL (20)), glucose variability, and CGM alarm settings, including hypoglycemia alarm (on/off), predictive hypoglycemia alarm (on/off), and glucose value set for hypoglycemia alarms (i.e., the glucose value at or below which the hypoglycemia alarm is triggered), were collected. In the current study, we defined significant level 2 hypoglycemia as presenting with $\geq 1\%$ of time in level 2 hypoglycemia (20).

Statistical Analysis

The sample size goal of 280 was calculated with the Cochran formula for achieving 95% CI and 5% margin of error, after assuming a pool of 1,024 potential participants. Descriptive statistics were used for demographics, diabetes durations, HbA_{1c} levels, BMI, eGFR, insulin pump/CGM use, Gold and A2A scores, and CGM glucose measures. The Mann-Whitney *U* test was conducted to

evaluate differences in age, diabetes duration, HbA_{1c} level, average CGM glucose level, percentage of time in hypoglycemia, glucose variability and glucose value set for hypoglycemia alarms, and Gold and A2A scores between participants with and without severe hypoglycemia in the past 6 months and with and without the presentation of significant level 2 hypoglycemia, as well as differences in A2A score between participants turning the CGM hypoglycemia alarm on and off. Logistic regression analysis was used to evaluate the odds ratio of severe hypoglycemia experience and significant level 2 hypoglycemia presentation with sex, with and without closed-loop insulin pumps, active CGM use time $\geq 70\%$ and $<70\%$, and turning on and off the CGM hypoglycemia alarm and predictive hypoglycemia alarm, as well as the odds ratio of severe hypoglycemia experience with significant level 2 hypoglycemia presentation. Linear regression analysis was conducted to evaluate the correlation between A2A score and glucose value set for hypoglycemia alarms. $P < 0.05$ was considered to be statistically significant.

RESULTS

Participant Demographics

A total of 320 surveys were initiated by participants, and 310 surveys were completed without duplications. No differences in age, HbA_{1c} level, BMI, or eGFR were found between participants and nonrespondents. A higher proportion of women (63.5%) completed the survey compared with nonrespondents (50.1%). After excluding participants using CGMs ≤ 6 months, 289 participants were included in analyses for severe hypoglycemia assessment (Table 1), and 257 participants with recent CGM data were included in analyses for CGM glucose assessment (Supplementary Fig. 1). Most of the participants were non-Hispanic Caucasians, and approximately one-third presented with IA. Also, most were using an insulin pump, with more than half using a pump with closed-loop features. In terms of CGM use, most participants were using Dexcom G6, and $>90\%$ had used CGMs for >1 year. Approximately 90% of participants were found to use CGMs at least 70% of the time, and most participants turned on hypoglycemia alarms (Supplementary Table

1). The mean time spent with glucose levels <70 and <54 mg/dL met the recommended goals, while the mean time spent with glucose levels >180 and >250 mg/dL exceeded the recommended goals (20).

Overall, 100 participants (34.6%) had either experienced severe hypoglycemia or presented with significant level 2 hypoglycemia, and nine participants (3.5%) had both severe hypoglycemia experience and significant level 2 hypoglycemia presentation.

Frequency and Risk Factors of Severe Hypoglycemia

A total of 74 (25.6%) of the 289 participants reported experiencing at least one episode of severe hypoglycemia in the past 6 months (Supplementary Fig. 2). Participants with severe hypoglycemia experience had higher HbA_{1c} and average CGM glucose levels, Gold scores, and glycemic variabilities (Fig. 1A). Participants presenting with significant level 2 hyperglycemia did not have higher risks for developing severe hypoglycemia ($P = 0.935$). Also, age, sex ($P = 0.864$), diabetes duration, time in hypoglycemia, not using a closed-loop insulin pump ($P = 0.081$), $<70\%$ active CGM use time ($P = 0.727$), turning off the hypoglycemia alarm ($P = 0.808$) and predictive hypoglycemia alarm ($P = 0.826$), and glucose value set for hypoglycemia alarms were not associated with experiencing severe hypoglycemia.

Regarding beliefs around hypoglycemia, the hyperglycemia avoidance prioritized theme summary score was higher in those who had experienced severe hypoglycemia ($P < 0.001$) (Fig. 2). For individual belief statements (Table 2), higher (i.e., statements 3, 5, 8, 9, 12) and lower (statements 10, 11) scores on certain statements were identified in participants with severe hypoglycemia.

Frequency and Risk Factors of Significant Level 2 Hypoglycemia

Of the 257 participants with recent CGM data, 237 (92%) were found to have spent some time in hypoglycemia (defined as glucose level <70 mg/dL), and 42 (16.3%) were found to have spent $\geq 4\%$ of time in hypoglycemia. Also, 172 participants (66.9%) were found to have spent some time in level 2 hypoglycemia, and 35 (13.6%) were

Table 1—Demographics and CGM profiles

Female sex	65
Age, years	45 ± 16
Race	
Caucasian	94
African American	3
Asian American	1
Other	2
Ethnicity	
Non-Hispanic	96
Hispanic	2
Unknown/refused	2
BMI, kg/m ²	29 ± 7
Diabetes duration, years	23.8 ± 13.9
HbA _{1c} , % (mmol/mol)	7.2 ± 1.0 (55 ± 11)
Patients with HbA _{1c} <7%	42
eGFR, mL/min/1.73 m ²	86 ± 20
Gold score for hypoglycemia awareness	3.0 ± 1.7
Normal	48
Impaired	33
Using insulin pump	80
With insulin auto-suspension feature	65
With closed-loop feature	61
Medtronic (670G, 770G)	9
Tandem (t:slim X2)	52
CGM type	
Dexcom G5	1
Dexcom G6	88
Medtronic Guardian	11
CGM use duration	
7–12 months	8
1–3 years	45
4–6 years	28
>6 years	19
Active CGM use time, %	89.5 ± 17.0
≥70% active use time	91
CGM glucose level, mg/dL	164 ± 31
Time with glucose >250, %	10.3 ± 11.0
Time with glucose >180, %	33.8 ± 19.0
Time with glucose 70–180, %	63.6 ± 17.9
Time with glucose <70, %	2.5 ± 3.3
Time with glucose <54, %	0.5 ± 1.0
CGM glucose variability, %	33.6 ± 5.3
Data are % or mean ± SD.	

found to have presented with significant level 2 hypoglycemia.

Participants presenting with significant level 2 hypoglycemia (Fig. 1B) were older, had lower HbA_{1c} and average CGM glucose levels, had higher Gold scores (i.e., lower hypoglycemia awareness), spent more time in hypoglycemia, had higher glycemic variabilities, were more likely to turn off the hypoglycemia alarm (odds ratio 3.57; $P = 0.007$) and predictive hypoglycemia alarm (odds

ratio 2.93; $P = 0.029$), and had lower glucose values set for hypoglycemia alarms (i.e., receiving glucose alarms at lower glucose levels). There were no relationships identified between significant level 2 hypoglycemia presentation and sex ($P = 0.510$), diabetes duration, <70% active CGM use time ($P = 0.068$), or not using a closed-loop insulin pump ($P = 0.343$).

Also, the summary score of the hypoglycemia concern minimized theme was

higher in those presenting with significant level 2 hypoglycemia. For individual belief statements (Table 2), higher scores on certain statements were identified in participants with significant level 2 hypoglycemia presentation (statements 4, 7).

For the relationship between A2A score and CGM hypoglycemia alarm settings, while no significant differences in A2A scores were identified between participants turning on and off the hypoglycemia alarm, higher scores on the minimizing hypoglycemia concerns theme were correlated with lower glucose values set for hypoglycemia alarms ($P = 0.012$).

CONCLUSIONS

Findings from the current study suggest the following in our sample of the population with type 1 diabetes who use advanced diabetes technologies: 1) more than one-third of individuals continue to experience severe hypoglycemia or spend a significant amount of time in level 2 hypoglycemia; 2) most individuals with relatively recent severe hypoglycemia do not necessarily present with significant level 2 hypoglycemia; 3) certain patient beliefs around hypoglycemia are associated with the development of severe and significant level 2 hypoglycemia, and beliefs that are related to severe hypoglycemia are distinct from those associated with significant level 2 hypoglycemia; and 4) while some risk factors for developing severe and significant level 2 hypoglycemia differ, IAH and high glucose variability continue to be associated with both of these dangerous hypoglycemic conditions.

The current study provides evidence that human behaviors continue to affect hypoglycemia outcomes in individuals with type 1 diabetes despite the implementation of advanced diabetes technologies. This study may also highlight the enduring importance of interventions for improving patient-driven hypoglycemia management (22), including the use of cognitive behavioral therapy-based psychological approaches to improve hypoglycemia self-management (26). This study demonstrated that beliefs around the theme hyperglycemia avoidance prioritized were associated with the development of severe hypoglycemia. In particular, individuals who

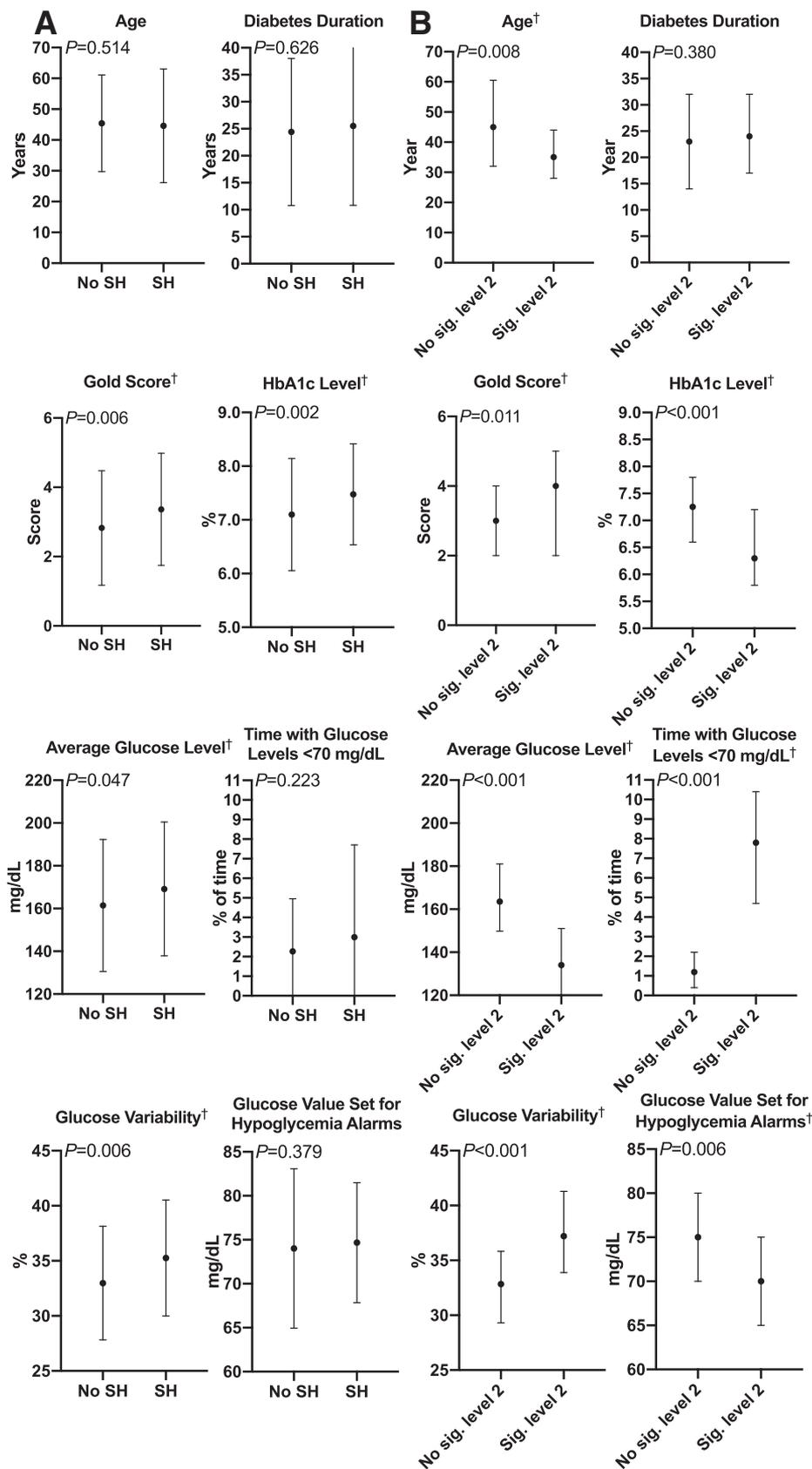


Figure 1—Demographics, diabetes and CGM glucose measures, and their associations with experiencing severe hypoglycemia (SH) in the last 6 months (A) and presenting with significant level 2 hypoglycemia, defined as spending $\geq 1\%$ of time in level 2 hypoglycemia (B). †Statistically significant.

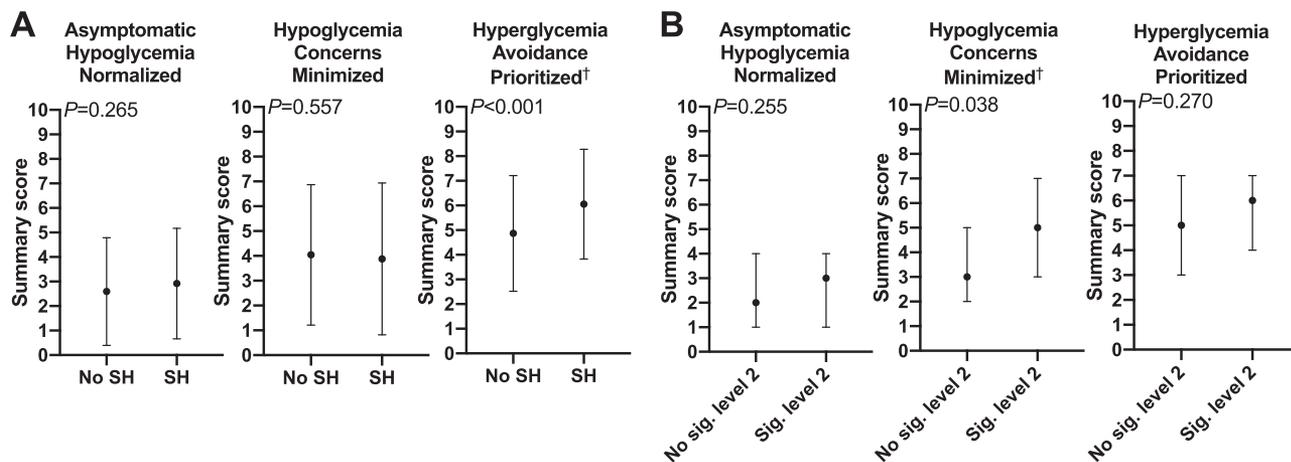


Figure 2—Summary scores on themes of beliefs around hypoglycemia and their associations with experiencing severe hypoglycemia (SH) in the last 6 months (A) and presenting with significant level 2 hypoglycemia, defined as spending $\geq 1\%$ of time in level 2 hypoglycemia (B). †Statistically significant.

reported “I get frustrated when I see high blood glucose readings” and “sometimes I know that I am giving myself more insulin than I really need” may be at risk for self-administering excessive bolus insulin doses in an attempt to more rapidly lower their glucose levels in response to hyperglycemia. In those with high average CGM glucose or HbA_{1c} levels, frequent feedback indicating hyperglycemia delivered through CGM devices including alarms could have further fueled or prompted these thoughts and behaviors, leading to administrations of excessive insulin doses followed by severe hypoglycemia.

On the other hand, individuals with stated beliefs such as “I can function okay with low blood glucose levels” and “there are no serious consequences to leaving mild hypoglycemia untreated” may underreact to hypoglycemia that either does not immediately compromise their function or presents with glucose levels that they consider not to be dangerously low. Also, the identified relationship between scoring higher on the minimizing hypoglycemia concerns theme and setting lower glucose values for hypoglycemia alarms provides evidence that individuals with minimal hypoglycemia concerns may alter their CGM hypoglycemia alarm settings to suppress some of these alarms. The resulting delay in hypoglycemia management can thus lead to more time spent in level 2 hypoglycemia.

In addition, setting the hypoglycemia alarm glucose value higher for early hypoglycemia alerts could help reduce

level 2 hypoglycemia (27). However, our findings suggest that this strategy may not sufficiently prevent severe hypoglycemia, which could be secondary to rapid drop in glucose levels resulting from insulin overbolusing. It also remains unclear why younger age is a risk factor for developing significant level 2 but not severe hypoglycemia. Further research is also needed to closely evaluate the role of age in patient-diabetes technology interactions, including alarm fatigue (28).

Individuals who reported severe hypoglycemia development within the last 6 months scored lower on several hypoglycemia concerns minimized statements, which may reflect fear of hypoglycemia that is possibly explained by their recent actual experiences of severe hypoglycemia. It remains unclear whether this presentation may protect against severe hypoglycemia by means of overriding beliefs comprising the prioritization of hyperglycemia avoidance theme. Furthermore, the mean scores on most beliefs tended to be $<50\%$ (i.e., <1.5) of the total maximal scores (of 3), suggesting that the beliefs do not need to be strong to indicate high risks for developing severe or significant level 2 hypoglycemia. This information could inform future behavioral intervention research, because it also implies that a small reduction in the belief scores may generate clinically significant benefits in terms of reducing hypoglycemia. The prominent exception to this pattern was the relatively high score for most individuals on frustration or worry about hyper-

glycemia. This finding suggests that concerns about or fear of hyperglycemia (29) could be common among these heavy users of diabetes technologies, who constantly receive real-time glucose feedback. Finally, it is important to note that the original study validating the A2A measure identified relationships between severe hypoglycemia and belief statements in a predominantly non-CGM-using population. Therefore, the implementation of advanced diabetes technologies may have mitigated some, but certainly not all, adverse impacts of hypoglycemia beliefs.

Surprisingly, the number of participants who had experienced severe hypoglycemia was higher than those presenting with significant level 2 hypoglycemia. There are several possible explanations for this observation. The continuous glucose information and alarms from CGMs may have increased individuals’ awareness of actual glucose levels and glucose targets, and the closed-loop feature has probably also helped mitigate some downtrend in glucose levels during hypoglycemia in pump users. These measures together could have helped reduce the time spent in level 2 hypoglycemia. On the other hand, because severe hypoglycemia may be driven by overbolusing, the closed-loop feature alone might not be sufficient to counteract the rapid decline in blood glucose levels with only reduction or suspension of basal insulin. The falsely high CGM glucose levels during hypoglycemia (30) could also contribute to underreporting of the time in level 2

Table 2—Scores on beliefs around hypoglycemia in patients with type 1 diabetes

Beliefs around hypoglycemia	Severe hypoglycemia			Significant level 2 hypoglycemia*		
	No	Yes	<i>P</i>	No	Yes	<i>P</i>
Asymptomatic hypoglycemia normalized						
1. I don't need to treat low blood glucose unless I feel symptoms	0.53 ± 0.84	0.49 ± 0.78	0.782	0.48 ± 0.82	0.69 ± 0.90	0.139
8. Treating hypoglycemia when I don't have symptoms is a bother to me	0.68 ± 0.89	1.03 ± 1.08	0.015†	0.74 ± 0.94	0.71 ± 0.89	0.958
2. I'd rather live life to the fullest than be too cautious about my diabetes	0.80 ± 0.85	0.80 ± 0.92	0.804	0.80 ± 0.86	0.80 ± 0.93	0.884
4. There are no serious consequences to leaving mild hypoglycemia untreated	0.59 ± 0.83	0.63 ± 0.83	0.616	0.50 ± 0.77	0.89 ± 0.87	0.004†
Hypoglycemia concerns minimized						
11. I don't get easily worried about hypoglycemia	1.25 ± 0.98	0.95 ± 1.06	0.017†	1.36 ± 0.98	1.29 ± 1.02	0.410
10. I don't believe I will have a severe hypoglycemic episode in the future	0.96 ± 1.04	0.38 ± 0.74	<0.001†	0.78 ± 0.98	0.69 ± 0.90	0.682
7. I can function okay with low blood glucose levels (i.e., <55 mg/dL)	0.65 ± 0.87	0.88 ± 1.06	0.156	0.57 ± 0.84	1.31 ± 1.13	<0.001†
5. Someone will always be around to help me if I have a low blood glucose episode	0.44 ± 0.84	0.66 ± 0.95	0.041†	0.45 ± 0.81	0.46 ± 0.92	0.801
Hyperglycemia avoidance prioritized						
9. I get frustrated and/or worried when I see high blood glucose readings	2.27 ± 0.89	2.57 ± 0.78	0.004†	2.36 ± 0.84	2.46 ± 0.85	0.422
6. It's more important to avoid having high blood glucose than going low	0.75 ± 0.88	1.01 ± 1.00	0.053	0.76 ± 0.89	1.00 ± 0.91	0.112
3. Good diabetes control is mainly about avoiding high blood glucose levels	1.18 ± 0.98	1.47 ± 1.05	0.041†	1.24 ± 1.00	1.14 ± 0.84	0.684
12. Sometimes I know that I am giving myself more insulin than I really need	0.68 ± 0.84	1.00 ± 0.95	0.007†	0.71 ± 0.84	0.86 ± 0.94	0.411

Data presented as mean ± SD and analyzed by Mann-Whitney *U* test. *Defined as spending ≥1% of time in level 2 hypoglycemia. †Statistically significant.

hypoglycemia. Furthermore, closed-loop insulin pump users were not found to experience less severe or significant level 2 hypoglycemia compared with CGM-only users in the current cohort, contrary to findings from prior clinical trials (10,11). These discrepant findings could be due to the fact that many individuals with high risks for developing dangerous hypoglycemia might have been initiated on closed-loop insulin pumps; this clinically adaptive strategy could have introduced selection bias in our study.

Observations from this study suggest that some of the traditional risk factors

for severe hypoglycemia development (31), including older age and longer diabetes duration, may not be applicable to users of advanced diabetes technologies. This observation is consistent with research in individuals with prolonged diabetes who use CGM technologies effectively to prevent hypoglycemia (32), and CGMs could possibly attenuate the risk to a level similar to that in other age/diabetes duration groups. Also, increasing evidence from recent years has suggested that controlled HbA_{1c} levels are not necessarily related to more severe hypoglycemia (33), while those with higher HbA_{1c}

levels or greater glycemic variabilities could actually experience more severe hypoglycemia episodes (34,35). These observations are consistent with our findings. In addition, as discussed above, CGM users may act differently from non-CGM users, because they constantly receive feedback on hyperglycemia, which could lead to insulin overbolusing behaviors.

Clinically, based on the current findings, advanced diabetes technologies alone do not help all individuals with type 1 diabetes eliminate severe hypoglycemia or reach hypoglycemia glucose goals. To reduce the burden of

hypoglycemia, our findings suggest that diabetes health care providers would need to address patient preconceived notions regarding prioritizing hyperglycemia avoidance and minimizing hypoglycemia concerns beyond prescribing CGMs and insulin pumps and providing basic training. Furthermore, while it may seem natural to assume that only individuals presenting with significant level 2 hypoglycemia would have a higher risk for developing severe hypoglycemia, our data suggest against this view and support universal screening for severe hypoglycemia using the indicator of any degree of hypoglycemia.

The current study has several strengths, including being one of the first studies to evaluate the impact of human behaviors on hypoglycemia in individuals using advanced diabetes technologies. This study recruited a representative sample size, with participant characteristics comparable to those of nonrespondents and with substantial portions of individuals using only CGMs and using CGMs with closed-loop insulin pumps. While participants had a higher proportion of women than nonrespondents, sex was not found to be a risk factor for developing severe or significant level 2 hypoglycemia. This study also assessed guideline-based hypoglycemia outcomes and used validated self-reported measures to evaluate how beliefs around hypoglycemia are related to hypoglycemia development. Also, only those using CGMs >6 months were included in the study to ensure sufficient experience with CGM use and that reported severe hypoglycemia occurred after CGM initiation.

The findings of the current study are mostly applicable to patient populations receiving care from the tertiary academic health center. Because this study may reflect a more challenging patient population referred from regional health care providers, the frequency of severe and level 2 hypoglycemia may be higher in participants compared with individuals seen at local centers. However, the University of Michigan Health System, as one of the largest health care complexes in Michigan, provides care to a population of >1 million people living in the Southeast Michigan community. In addition, the racial/ethnicity and insulin pump use ratios of the participants were similar to those in the 2016–2018 T1D Exchange national report (19), and recent large-

scale, real-world research also suggests that 13.7–17.7% of individuals using CGMs develop significant level 2 hypoglycemia (36), consistent with our data. Our results therefore may also be generalizable to other diabetes centers. In the current study, the level 2 hypoglycemia measures from Medtronic CGM users were based on glucose levels <50 mg/dL, and this may have led to underreporting of the time spent in level 2 hypoglycemia. Also, recent data suggest that a single hypoglycemia awareness questionnaire alone may not accurately predict autonomic symptom status as determined with hypoglycemia clamps (37). However, the Gold questionnaire is a simple tool for hypoglycemia awareness assessment and could be easily implemented in clinical practice. Finally, insulin bolus dose information was not collected as a part of the study protocol; future research is necessary to prove the concept of insulin overbolusing as the cause of severe hypoglycemia in this population.

In conclusion, dangerous hypoglycemia continues to occur in individuals with type 1 diabetes, despite the implementation of advanced diabetes technologies. Additionally, human factors, including beliefs around hypoglycemia, may continue to have an impact on the effectiveness of glucose self-management in this group.

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full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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